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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/454,737	12/06/99	PERRICAUDET M	8076.85USC1

023552
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HM12/0621

EXAMINER	
GUZO,D	
ART UNIT	PAPER NUMBER
1636	19

DATE MAILED: 06/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/454,737	PERRICAUDET ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15, 18-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

ZETA ADAMS
PATENT ANALYST
Zeta Adams

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perricaudet et al. in view of Quantin et al. and Rice et al.

Applicants claim a composition comprising a recombinant non-replicative adenoviral vector composition comprising a polynucleotide sequence encoding a heterologous protein (which can be all or part of a dystrophin gene product or a β-galactosidase gene product) inserted into a

deleted E1 region of the vector and under control of a RSV LTR promoter and a pharmaceutically acceptable carrier and wherein the gene product is expressed in muscle cells.

Perricaudet et al. (Cited by applicants, see whole article, particularly Figs. 2-3 and pp. 56-57) recites the generation of recombinant non-replicative adenoviral vectors wherein heterologous coding sequences are inserted into a deleted E1 region of the virus. Perricaudet et al. also recites the use of recombinant adenovirus vectors (combined with a pharmaceutically acceptable carrier) to deliver genes of interest (i.e. β-galactosidase) into muscle cells *in vivo*. Perricaudet et al. does not recite use of the RSV LTR promoter to drive expression of the heterologous coding sequence and does not specifically recite a sequence coding for all or part of a dystrophin gene.

Quantin et al. (Cited by applicants, see whole article) recites generation and use of replication defective adenovirus vectors for use in expressing genes (i.e. encoding β-galactosidase) in muscle cells *in vivo*. Quantin et al. also recites that adenoviral vectors can be used to direct expression of sequences encoding dystrophin in muscle cells.

Rice et al. (Nature, Vol. 332, 1988, pp. 551-553, see whole article, particularly p. 551) discloses use of the RSV LTR promoter to direct heterologous gene expression in E1 region deleted recombinant non-replicative adenoviral vectors.

The skilled artisan, seeking to generate a recombinant non-replicative adenovirus vector for use in expressing genes in muscle cells, would have been motivated to use the teachings of Perricaudet et al. and Quantin et al. on the generation of recombinant, replication deficient,

adenoviral vectors capable of expressing genes of interest (which can include dystrophin) in muscle cells with the teachings of Rice et al. on use of the well known and characterized strong promoter from the RSV LTR to drive expression of heterologous genes in cells in order to generate a replication defective adenoviral vector deleted in the E1 region and comprising a coding sequence for β-galactosidase (as a marker) or dystrophin inserted into the deleted E1 region and under control of the strong RSV LTR promoter. It would have been obvious for the ordinary skilled artisan to do this because Perricaudet et al. and Quantin et al. recite the desirability of using replication defective adenoviral vectors (deleted in the E1 region) for introducing genes, which can be markers or of therapeutic benefit (which can include dystrophin) into muscle cells and Rice et al. teaches the use of the well known strong RSV LTR promoter to drive expression of a heterologous gene in an adenoviral vector deleted in the E1 region. One of ordinary skill in the art would have been motivated to use a well known strong promoter such as the RSV LTR to direct expression of the heterologous gene in an adenoviral vector (as taught by Perricaudet et al. and Quantin et al.) so as to ensure high levels of expression of the gene product. Given the teachings of the cited art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be assumed that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over

Perricaudet et al. in view of Rice et al. and Nabel et al.

Applicants claim a composition comprising an E1 deleted non-replicative adenoviral vector comprising a heterologous nucleic acid sequence encoding a protein with thrombolytic properties and under control of the RSV LTR promoter and wherein said composition also comprises a pharmaceutically acceptable carrier.

Perricaudet et al. is applied as in the above 35 USC 103(a) rejection of claims 15 and 18-19. Perricaudet et al. does not recite use of the RSV LTR promoter to drive expression of a sequence encoding a protein with thrombolytic properties.

Rice et al. is applied as in the above 35 USC 103(a) rejection of claims 15 and 18-19.

Nabel et al. (U.S. Patent 5,328,470, issued 7/12/94, filed 7/26/91, see whole document, particularly Column 4, lines 40-68 and Columns 5, 8-9 and 11) recites the use of adenoviral vectors to express genes with thrombolytic properties (i.e. plasminogen activator, streptokinase, etc.) in muscle cells *in vitro* or *in vivo* so as to treat ischemic disease, etc.

The ordinary skilled artisan, seeking to develop a adenoviral vector for expression (in muscle cells) of a protein with thrombolytic properties would have been motivated to combine the teachings of Perricaudet et al. on the generation of adenoviral vectors deleted in the E1 region and the desirability of their use to deliver genes of interest to muscle cells with the teachings of Rice et al. on the use of the RSV LTR promoter to drive expression of heterologous genes in E1 deleted adenoviral vectors and further with the teachings of Nabel et al. on the use of adenoviral vectors

to deliver sequences (to muscle cells) encoding thrombolytic proteins such as plasminogen activator and streptokinase to target cells and generate a E1 deleted adenoviral vector capable of expressing an inserted nucleotide sequence in muscle cells, said inserted sequence encoding a protein with thrombolytic properties, said sequence under control of the RSV LTR promoter. It would have been obvious for the ordinary skilled artisan to combine the teachings of Perricaudet et al. with Nabel et al. because both deal with use of adenoviral vectors to deliver genes of interest to muscle cells. Furthermore, the ordinary skilled artisan would have chosen the RSV LTR promoter because this promoter was a well known strong promoter operable in recombinant adenoviral vectors and was capable of expressing heterologous genes of interest at high levels (Rice et al.). Given the teachings of the cited art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15 and 17-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,099,831. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods for delivering to muscle cells a recombinant adenoviral vector claimed in the '831 patent utilize the same recombinant adenoviral vectors claimed in the instant application. The instantly claimed adenoviral vectors are essential for practicing the claimed methods of delivering genes to animal and human muscle cells recited in the '831 patent and would be obvious in view of the patented method claims. One of ordinary skill in the art would have been motivated to generate the instantly claimed adenoviral vectors because said vectors are essential for practicing the claimed method recited in the '831 patent. It would have been obvious for the ordinary skilled artisan to do this because the instantly claimed adenoviral vectors are essential for practicing the claimed methods of delivering genes to muscle cells recited in the '831 patent. Given the teachings of the claims in the '831 patent and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be assumed that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15 and 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 (and dependent claims) are vague in the recitation of "a" promoter of the RSV LTR or "a" promoter of the IE gene of CMV, etc. Use of "a" implies that the promoter is chosen from among several promoters of the RSV LTR or IE gene of CMV, etc. It is unclear if there is more than one promoter in the recited entities since standard terminology refers to **the** CMV IE promoter or **the** RSV LTR promoter, etc. It is unclear which specific promoter is being referred to, i.e. how many promoters are contained in the RSV LTR and which one is being chosen. Redrafting the claim to recite a promoter selected from "the" RSV LTR, "the" CMV IE promoter, etc. would be remedial.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting

supervisor, Robert Schwartzman, can be reached on (703) 308-7307. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

David Guzo
June 19, 2001

DAVID GUZO
PRIMARY EXAMINER